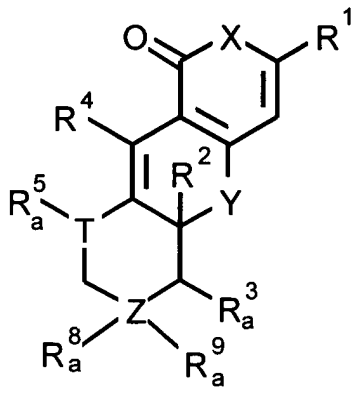
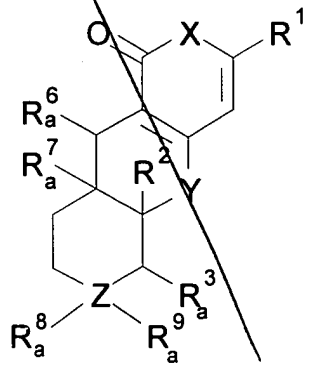
CLAIMS

We claim:

1. A method of treating a symptom or condition that results from the activity of aldose reductase comprising administering to a patient an effective amount of one or more compounds of the formula:



or



wherein:

T is independently CR, NR, N, S or O;

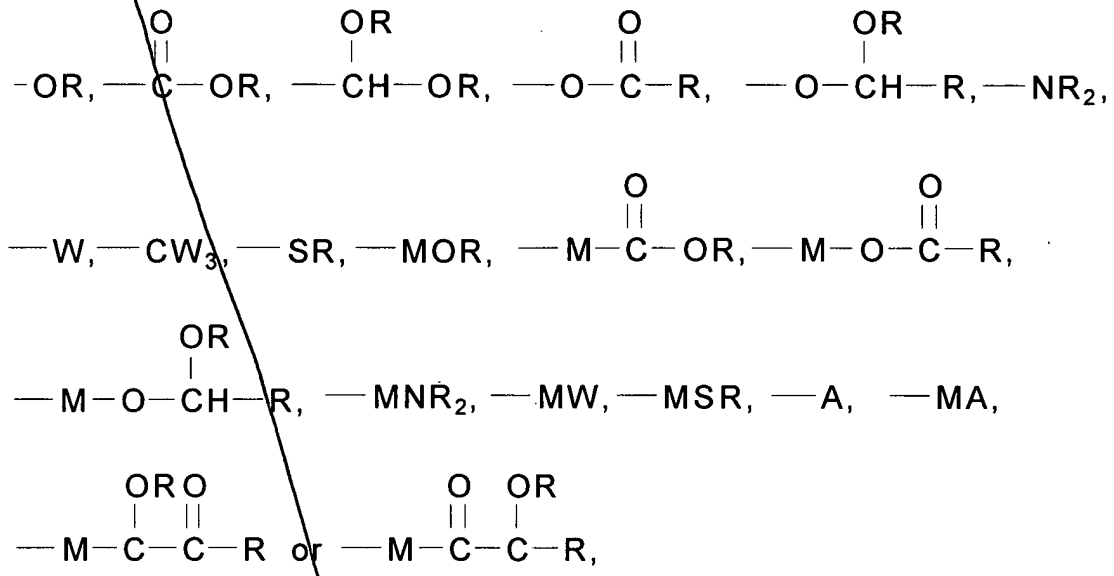
X is independently O, NR, N or S;

Y is independently O, NR, N or S;

Z is independently C, N, S or O;

a is 0 or 1;

R^1, R^3, R^4 and R^5 are, independently, R,



wherein R is independently H, OH, alkyl, alkenyl or alkynyl, an aromatic ring system, amino, sulfhydryl, or sulfonyl, M is a divalent alkyl, alkenyl or alkynyl, aromatic ring system, or sulfonyl, W is Cl, F, Br or OCl, and A is an aromatic ring system;

R^2, R^8 and R^9 are independently R as defined above; and

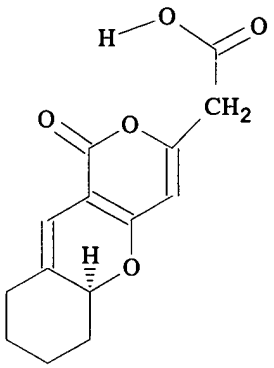
R^6 is independently R, NH_2, OH, or OCOR where R is as set forth above;

R^7 is independently OH or H; or

R^6 and R^7 taken together are O;

and pharmaceutically acceptable salts or esters of the foregoing, as well as optical isomers thereof.

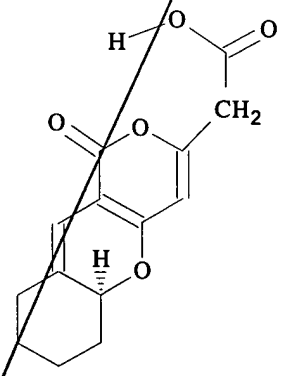
2. The method of claim 1, wherein said patient is a dog and said compound is:



3. The method of claim 2, wherein the compound is administered orally.

4. The method of claim 2, wherein the compound is administered topically.

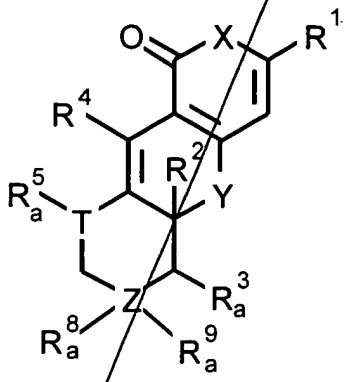
5. The method of claim 1, wherein said patient is a human and said compound is:



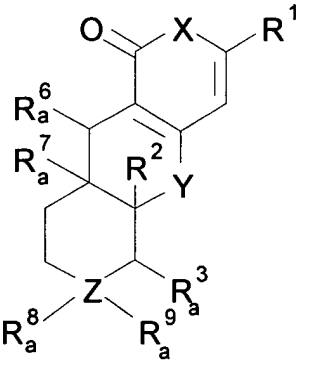
6. The method of claim 5, wherein the compound is administered orally.

7. The method of claim 5, wherein the compound is administered topically.

8. A method of inhibiting aldose reductase activity in cells, comprising contacting the cells with an effective amount of a compound of formula:



or



wherein:

T is independently CR, NR, N, S or O;

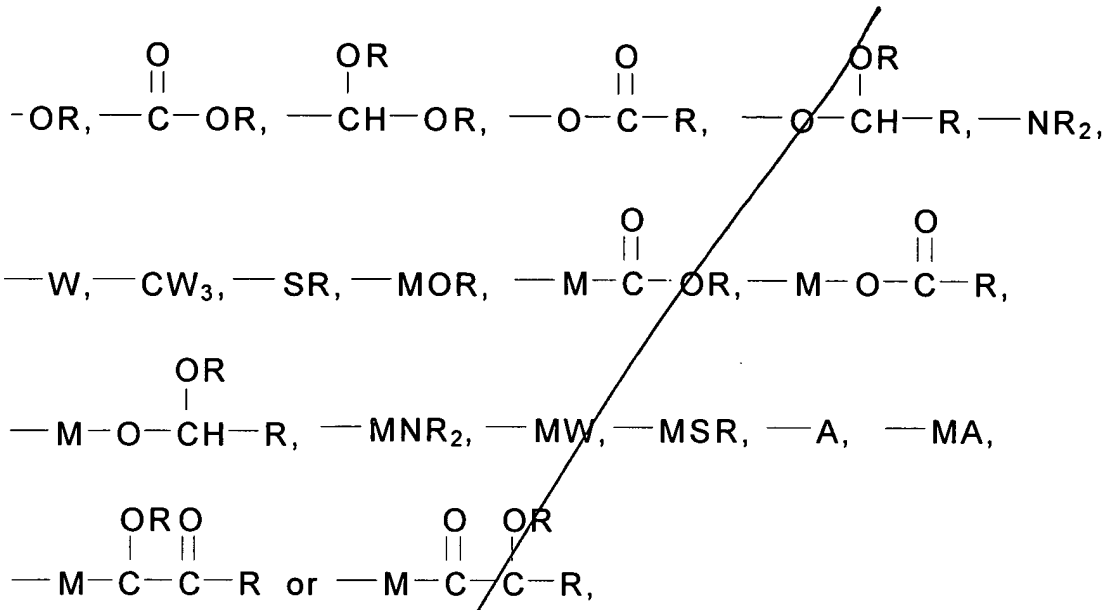
X is independently O, NR, N or S;

Y is independently O, NR, N or S;

Z is independently C, N, S or O;

a is 0 or 1,

R^1, R^3, R^4 and R^5 are, independently, R,



wherein R is independently H, OH, alkyl, alkenyl or alkynyl, an aromatic ring system, amino, sulfhydryl, or sulfonyl, M is a divalent alkyl, alkenyl or alkynyl, aromatic ring system, or sulfonyl, W is Cl, F, Br or OCl, and A is an aromatic ring system;

R^2, R^8 and R^9 are independently R as defined above; and

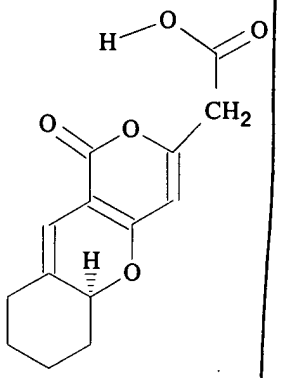
R^6 is independently R, NH_2, OH, or OCOR where R is as set forth above;

R^7 is independently OH or H; or

R^6 and R^7 taken together are O;

and pharmaceutically acceptable salts or esters of the foregoing, as well as optical isomers thereof.

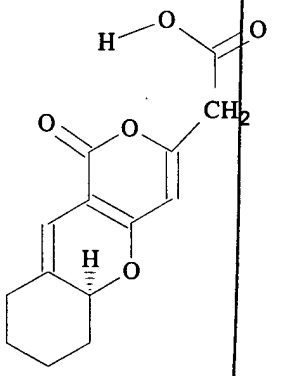
9. The method of claim 8, wherein said patient is a dog and said compound is:



10. The method of claim 9, wherein the compound is administered orally.

11. The method of claim 9, wherein the compound is administered topically.

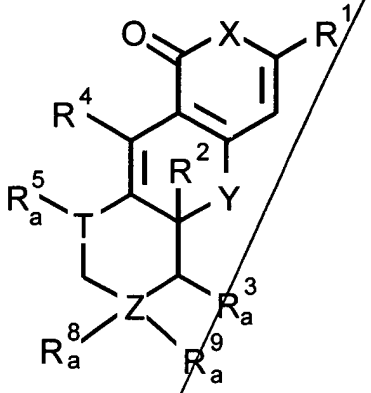
12. The method of claim 8, wherein said patient is a human and said compound is:



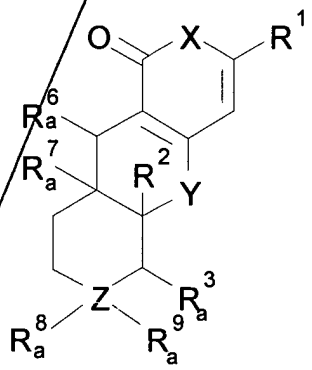
13. The method of claim 12, wherein the compound is administered orally.

14. The method of claim 12, wherein the compound is administered topically.

15. A method of treating retinopathy comprising:
administering to a patient an effective amount of a compound of formula:



or



wherein:

T is independently CR, NR, N, S or O;

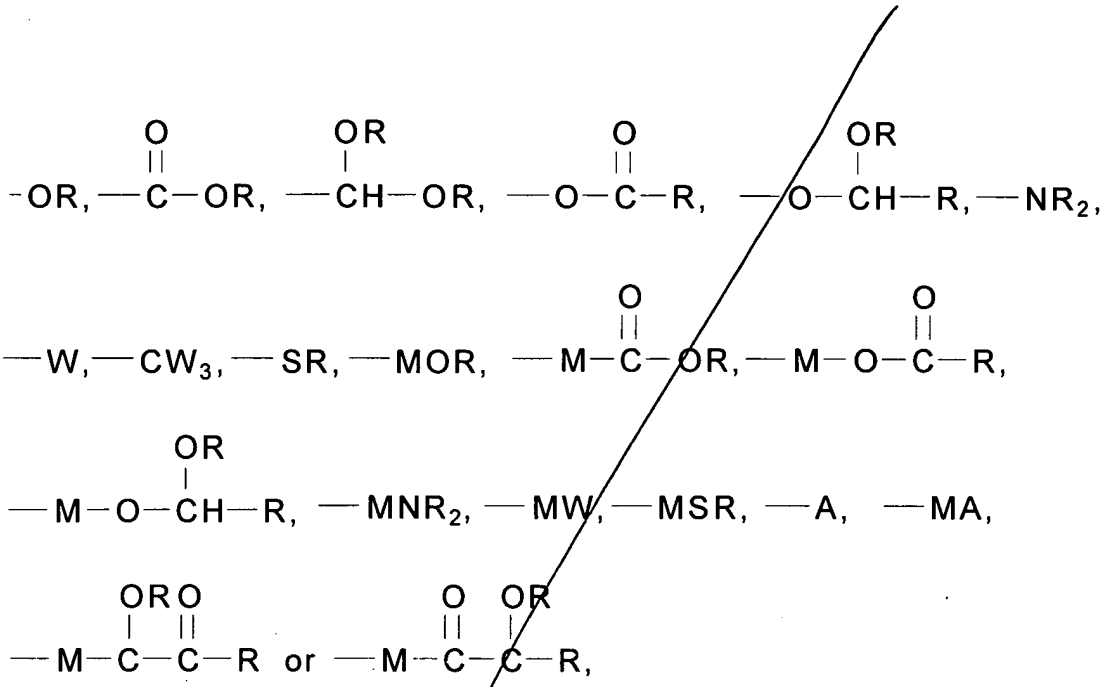
X is independently O, NR, N or S;

Y is independently O, NR, N or S;

Z is independently C, N, S or O;

a is 0 or 1,

R^1, R^3, R^4 and R^5 are, independently, R,



wherein R is independently H, OH, alkyl, alkenyl or alkynyl, an aromatic ring system, amino, sulfhydryl, or sulfonyl, M is a divalent alkyl, alkenyl or alkynyl, aromatic ring system, or sulfonyl, W is Cl, F, Br or OCl, and A is an aromatic ring system;

R^2, R^8 and R^9 are independently R as defined above; and

R^6 is independently R, NH_2, OH, or OCOR where R is as set forth above;

R^7 is independently OH or H; or

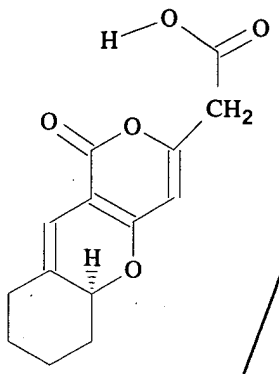
R^6 and R^7 taken together are O;

and pharmaceutically acceptable salts or esters of the foregoing, as well as optical isomers thereof.

16. The method of claim 15, wherein the compound is administered orally.

17. The method of claim 15, wherein the compound is administered topically.

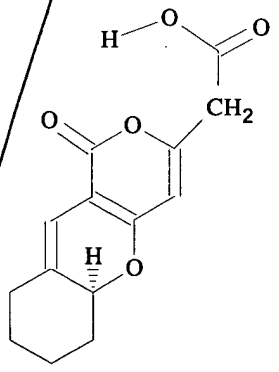
18. The method of claim 15, wherein said patient is a dog, and said compound is



19. A method of decreasing the loss of PKC in diabetic patients comprising administering to a patient an effective amount of one or more compounds of claim 1.

20. A method of inhibiting polyol accumulation in diabetic patients comprising administering to a patient an effective amount of one or more compounds of claim 1.

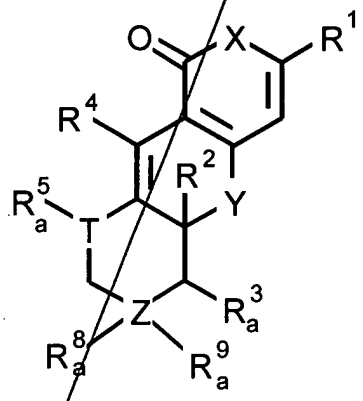
21. A pharmaceutical composition comprising a compound with formula:



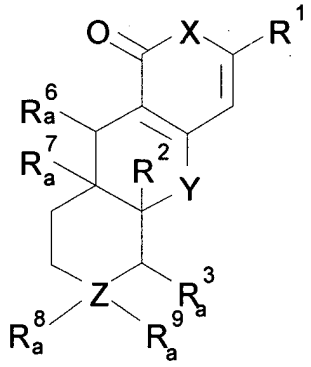
wherein the compound is useful to treat a disorder associated with the activity of aldose reductase.

22. A method of preparing a pharmaceutical composition comprising:

bringing a compound of formula:



or



wherein:

T is independently CR, NR, N, S or O;

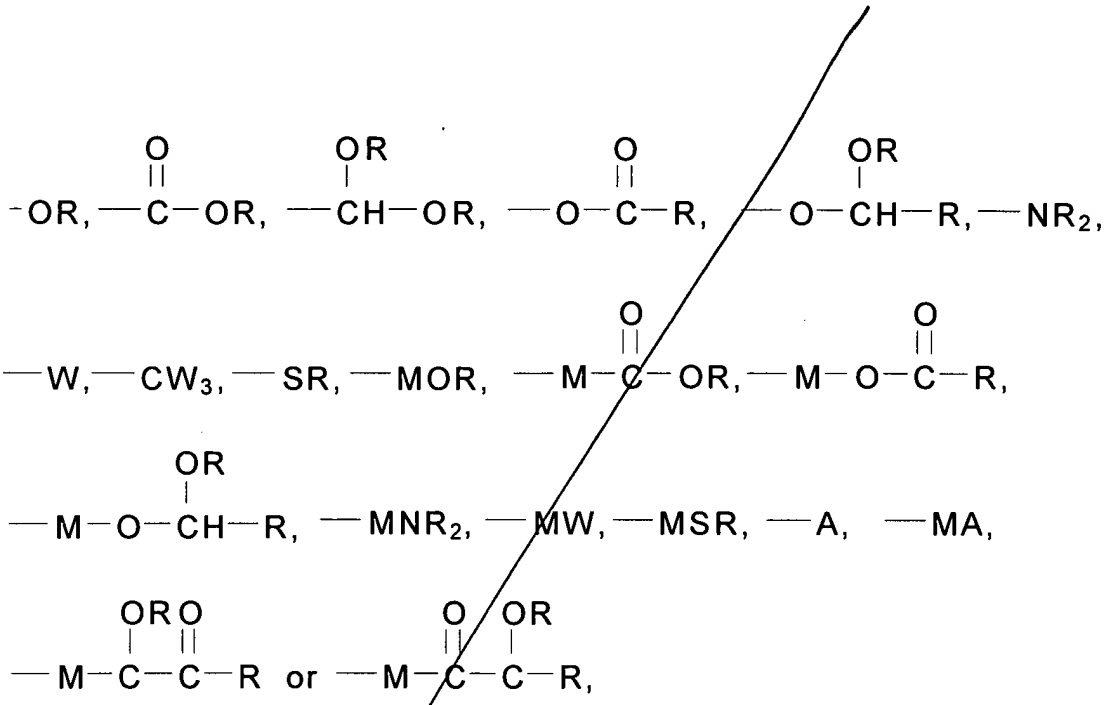
X is independently O, NR, N or S;

Y is independently O, NR, N or S;

Z is independently C, N, S or O;

a is 0 or 1,

R^1, R^3, R^4 and R^5 are, independently, R,



wherein R is independently H, OH, alkyl, alkenyl or alkynyl, an aromatic ring system, amino, sulfhydryl, or sulfonyl, M is a divalent alkyl, alkenyl or alkynyl, aromatic ring system, or sulfonyl, W is Cl, F, Br or OCl, and A is an aromatic ring system;

R^2, R^8 and R^9 are independently R as defined above; and

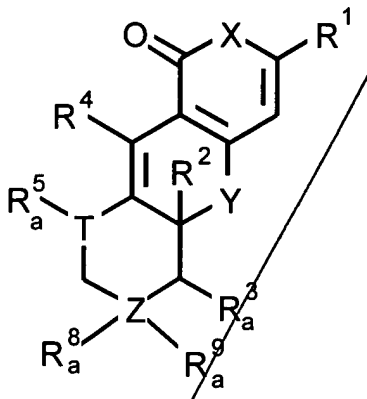
R^6 is independently R, NH_2, OH, or OCOR where R is as set forth above;

R^7 is independently OH or H; or

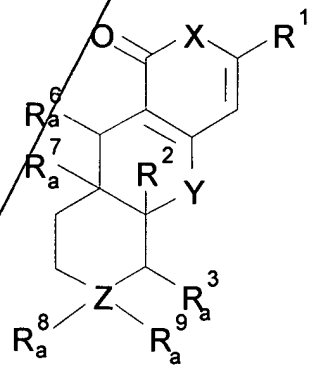
R^6 and R^7 taken together are O;

and pharmaceutically acceptable salts or esters of the foregoing, as well as optical isomers thereof, into association with a pharmaceutically acceptable carrier.

23. A compound selected from the group consisting of compounds of formula:



or



wherein:

T is independently CR, NR, N, S or O;

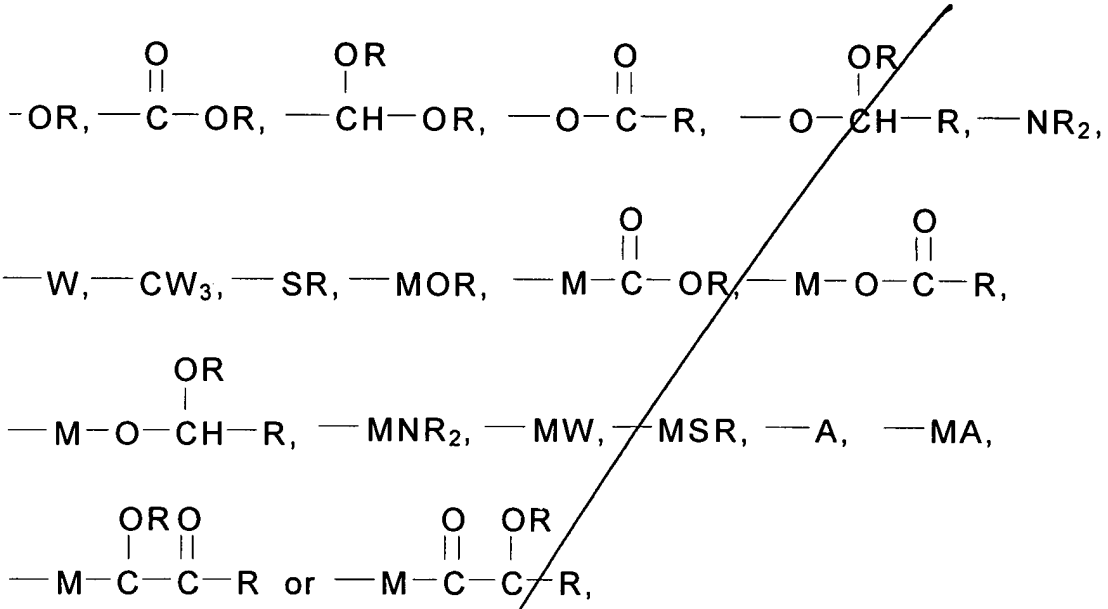
X is independently O, NR, N or S;

Y is independently O, NR, N or S;

Z is independently C, N, S or O;

a is 0 or 1,

R^1, R^3, R^4 and R^5 are, independently, R,



wherein R is independently H, OH, alkyl, alkenyl or alkynyl, an aromatic ring system, amino, sulfhydryl, or sulfonyl, M is a divalent alkyl, alkenyl or alkynyl, aromatic ring system, or sulfonyl, W is Cl, F, Br or OCl, and A is an aromatic ring system;

R^2, R^8 and R^9 are independently R as defined above; and

R^6 is independently R, NH_2, OH, or OCOR where R is as set forth above;

R^7 is independently OH or H; or

R^6 and R^7 taken together are O;

provided that either:

T is independently CR, provided that R is not H, or NR;

X is independently NR or N, provided that R is not H;

Y is independently NR, provided that R is not H; or

R^1, R^3, R^4 and R^5 are, independently,

-CH(OR)-OR; -O-CH(OR)-R; -M-O-CH(OR)-R; -M-C(OR)-C(=O)-R; or -M-C(=O)-C(OR)OR.